adjuvant anti-tumor effect of PSA-specific T cells. This report presents a novel treatment approach involving allogeneic SCT in prostate cancer patients who do not respond to chemotherapy and/or cannot undergo prostectomy.

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PERIPHERAL BLOOD STEM CELLS AND GRANULOCYTE COLONY-STIMULATING FACTOR ARE ASSOCIATED WITH ACUTE GRAFT-VERSUS-HOST DISEASE

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Does granulocyte colony-stimulating factor (G-CSF) increases GVHD or not? A mouse model of GVHD showed that G-CSF induce GVHD after bone marrow (BM) transplantation (Morris et al, Nature Med 15:436, 2009). Total body irradiation (TBI) increased G-CSF receptors on host dendritic cells, stimulating acute GVHD. Their report prompted us to reassess the role of G-CSF prophylaxis in our HSCT patients. During 1994–2002, 260 patients were given G-CSF prophylaxis. Patients not given G-CSF (n = 205) who underwent HSCT from 1993 to 2003 were controls. We included all patients receiving BM (n = 286) or peripheral blood stem cell (PBSC) grafts (n = 179) from HLA-identical siblings (n = 225) or HLA-A, -B, or DRß1 genomically identical unrelated donors (MUDs; n = 240). The G-CSF group had more MUD transplants, fewer patients receiving reduced-intensity conditioning (RIC), more patients receiving antithymocyte globulin ($p < 0.001$), and AB0 mismatch was commoner ($p = 0.03$). Patients treated with G-CSF had acute GVHD (grades II–IV) of 29%, vs. 19% in the controls ($p < 0.01$). GVHD occurred in 33% of patients given PBSC, as compared to 19% of those given BM ($p < 0.001$). There was no significant difference in incidence of GVHD between HLA-identical sibling transplants and MUD transplants, between those with myeloablative conditioning and those with RIC, or between those treated with TBI and chemotherapy and those treated with chemotherapy only. In patients conditioned with chemotherapy, 34% in the G-CSF group developed acute GVHD as compared to 21% in the controls ($p = 0.035$). In patients treated with TBI, those given G-CSF had an incidence of acute GVHD (grades II–IV) of 26% as opposed to 17% in the controls ($p = 0.10$). In PBSC recipients, 39% in the G-CSF group developed acute GVHD as compared to 24% in the controls ($p = 0.025$). In recipients of BM, the corresponding figures were 22% and 15%, respectively, in the two groups ($p = 0.19$). In the present study, a multivariate analysis showed that acute GVHD of grades II–IV was associated with PBSC grafting (hazards ratio (HR) = 2.29, $p < 0.0001$), female donors (HR = 1.74, $p = 0.005$), major AB0 mismatch (HR = 1.58, $p = 0.03$), and G-CSF (HR = 1.52, $p = 0.03$). Differences were adjusted. There were no differences between the two groups regarding non-relapse mortality, relapse, and survival.

Conclusion: G-CSF induces GVHD in mice, but differs compared to humans regarding the role of source of stem cell and conditioning regimen.

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SIROLIMUS, TACROLIMUS, AND RABBIT ATG (RATG) AS GRAFT-VERSUS-HOST PROPHYLAXIS IN PATIENTS UNDERGOING UNRELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANT (HCT)

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The use of sirolimus combined with tacrolimus +/- low-dose methotrexate (MTX) recently showed a promising result in preventing acute GVHD after unrelated donor HCT (Antin et al. Blood 2003) although a significant number of patients still experienced chronic GVHD. In an attempt to further improve the outcome, we have developed a novel combination of tacrolimus (FK), sirolimus (SIR) and r-ATG +/- MTX (MTX given for patients with a mismatch donor) and studied in a total of 51 patients who underwent unrelated donor HCT from 7/5/2006 to 7/31/2009. The median age at transplant was 56 (range: 16 -71). Twenty were female and 31 were male. Indications for transplant were as follows: ALL (n = 12, CR1/2 = 11, Induction Failure = 1), AML (n = 19: CR1/2 = 12: relapse/induction failure = 7), CML (n = 4: CP1/2 = 2, AP/BC = 2), non-Hodgkin Lymphoma (n = 5); CLL (n = 1), MDS (n = 8), MPD (n = 2). Thirty one patients received reduced-intensity conditioning (fludarbine/melphalan [Flu/Mel]) and 20 received full-intensity conditioning (FTBI/VP-16: n = 13, FTBI/Cytoxan: n = 7). All received PBSC graft except for two patients who received bone marrow graft. Twenty-nine of 51 patients had a 10/10-match donor by high resolution HLA typing. Engraftment rate was 92.2% (n = 47) with the median neutrophil engaftment at 15 days (range: 10-39). Eighteen patients (38% of 47 engrafted) developed grade II-IV acute GVHD (grade III = 3, grade IV = 0). Chronic GVHD developed in 21 of 37 evaluable patients (57%, limited n = 7, extensive n = 14). We observed TTP/HUS in 10 patients (20%) and one case of VOD. Eighteen (42%) of 43 patients at risk (R+ or D+) developed CMV reactivation, while 10 patients developed EBV reactivation (19.6%). After a median follow up of 11 months (range: 2-35) 38 patients were alive. The 1-year probabilities of overall survival, disease-free survival (DFS), and relapse rate were 74.7% (63-83%), 73.2% (62-82%), and 11% (5-25%), respectively. Non-relapse mortality was 14.7% (8-26%) at 100 day and 17.5% (10-29%) at 1 year. There were no significant differences in the outcomes according to conditioning regimens, although there was a trend for lower NRM with Flu/Mel (11% vs. 27% at 1 year, $p = 0.1$).

In summary FK/SIR combined with r-ATG +/- MTX is associated with a promising early result in GVHD prevention and survival in this high-risk population. However, the rate of graft failure (n = 4) appeared greater than our historic data, which is being further investigated at our institution.

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PROGRESSIVE IMPROVEMENT IN STEROID-REFRACTORY/DEPENDENT/INTOLERANT CUTANEOUS CHRONIC GRAFT-VERSUS-HOST DISEASE (CGVHD) FOLLOWING A 24-WEEK COURSE OF EXTRACORPOREAL PHOTOPHERESIS (ECP)

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In a previously reported multicenter randomized standard-therapy controlled trial, a 12-week course of ECP resulted in several beneficial outcomes in patients (pts) with steroid-refractory/intolerant/dependent cGVHD. (Flowers et al, Blood 112:2667-74. 2008). We conducted an open-label cross-over extension study to provide access to ECP for participants in the standard of care arm of this randomized study and enrolled 29 pts. ECP was administered 3 times during week 1, 2 treatments weekly until week 12 then 2 treatments until week 24. The median age of the study cohort was 43 (20-67) years and 26 pts (90%) had extensive cGVHD. Onset was *de novo* in 11 (37.9%), progressive in 15 (51.7%) and quiescent in 3 (10.3%). Twenty-five of 29 pts (86%) completed the 24 week course of ECP open-label treatment. Causes for not completing the 24-weeks were GVHD progression (n = 2), 1 suicide, and 1 withdrawal of consent. Mean daily steroid dose was 18.4 mg at the first ECP visit in this extension study (baseline). The median total skin score (TSS) was 7.8 (1.0-18.5) at the start of this cross-over extension study. The median percent change in TSS from baseline to week 12 and week 24 was -8.0 and -22.7, respectively. Four pts (14%) and 7 pts (24%) achieved a ≥50% reduction in steroid dose at weeks 12 and 24, respectively. In 4 pts (14%) and 8 pts (28%) a ≥50% reduction in steroid dose and a final steroid dose of <10 mg/day at weeks 12 and 24 was obtained respectively. Complete or partial skin response at week 24 was observed in 4 pts (14%) by investigator assessment.